32. (NEW) The antibody of claim 31, wh rein the antibody fragment is Fab, $F(ab')_2$, Fv or single chain Fv.

33. (NEW) The antibody of claim 31, wherein the antibody is a chimeric, humanized, deimmunised or human.

34. (NEW) A cell line producing the antibody or binding fragment of claim 31.

35. (NEW) A cell line producing the chimeric Fab fragment of claim 32.

36. (NEW) The chimeric form of the antibody of claim 31, having a mouse variable region and a human constant region, of the monoclonal antibody 166-32.

37. (NEW) The chimeric form of the antibody of claim 31, having a mouse variable region and a human constant region, of the Fab fragment of the monoclonal antibody 166-32.

38. (NEW) A method of treating a disease or condition mediated by excessive or uncontrolled activation of the complement system comprising administering, *in vivo* or *ex vivo*, an effective amount of the inhibitor according to claim 22 to block excessive or uncontrolled activation of the complement system.

39. (NEW) The method according to claim 38, wherein the inhibitor is administered to a patient undergoing cardiopulmonary.

40. (NEW) The method according to claim 39, wherein the inhibitor is administered *in vivo*.

41. (NEW) The method according to claim 39, wherein the inhibitor is administered *ex vivo*.

REMARKS

Applicants have cancel d claims 1-21 and added new claims 22-41 to more particularly and distinctly claim the invention. Support for new claims 22-41 may be

found in the specification as a whole and claims 1-21 specifically. No new matter has been introduced by this amendment. Even though claims 39-41 are directed to a non-elected invention, Applicants request that these claims be entered and cancellation held in abeyance until allowable subject matter is identified and rejoinder can be requested.

I. Formal Matters

Applicants have submitted a substitute page 24 as requested by the Examiner to correct a printing error. New page 24 does not introduce new matter, but merely replaces the existing page with corrected margins.

II. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-9 and 12 have been rejected as lacking written description for inhibitor other than antibodies. In view of the cancellation of these claims, this rejection is rendered moot. Applicants submit that this rejection does not apply to the antibodies of claims 22-37 in view of the Examiner's statement in paragraph 6 of the Office Action.

Claims 10-19 have been rejected as lacking enablement without the deposit of the murine hybridoma (Accession No. HB12476) that produces MAb. Applicant's representative hereby states that the deposit of HB12476 was made under the terms of the Budapest Treaty and, upon issuance of a patent from this application, all restrictions imposed upon the depositor will be irrevocably removed, except the requirement to notify the patentee of a request for the deposited material. In view of this statement, Applicants submit that this rejection should not apply to new claims 29-37.

III. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 13-14 and 16-17 have been rejected as being indefinite. In view of the cancellation of th se claims, this rejection is rendered moot. Applicants submit that this rejection does not apply to the antibodies of claims 22-39.

IV. Rejection Under 35 U.S.C. § 102

A. Claims 1-7 and 12 have been rejected as anticipated by Pascual et al. (J. Immunol. Methods 127:263-269 (1990). The Office asserts that "Pascual et al. teach a monoclonal antibody that binds factor D and completely inhibits rabbit erythrocyte hemolysis by human serum as well as prevents cleavage of C3 to C3b by cobra venom factor at a ratio of 80:1" (Office Action Page 4, first paragraph). This rejection is rendered moot by the cancellation of claims 1-19. However, Applicants respectfully submit that this rejection does not apply to new claims 22-37 (or claims 38-41).

Applicants draw the Examiner's attention to the last paragraph of the reference. The authors clearly state "[t]o obtain complete blockade of human factor D required a molar ratio of Mab to factor D of 80:1. More efficient Mabs are needed." The authors admit that their antibodies are not able to completely block complement inhibition at a ratio of less than 80:1, much less at such the substantially lower ratio of 1.5:1 required by the present claims. Contrary to the Office's assertion, it is clear that the antibodies of claims 22-37 are not the same as the antibodies of the cited reference otherwise it would not **require** such a significant amount of antibody to inhibit complement activation. In order to inhibit complement activation at a ratio of 1.5:1, the binding affinity of the antibodies must be significantly higher than those of the cited reference. Binding affinity is not an "inherent property" attributable to all antibodies as being equal, in view of the nature of dissociation constants. As stated in the specification at page 26, antibodies exemplified have a K_D of less than 0.1 nM. Although the authors do not disclose what the K_D of their Mabs is, it must be significantly higher in view of the need to add antibody to a ratio of 80:1 in order to obtain complete complement inhibition.

In view of this discussion, Applicants submit that Pascual et al. do not anticipate claims 22-37.

B. Claims 1-4 and 7 have been rejected as anticipated by Sahu et al. This rejection was rendered moot by the cancellation of claims 1-19.

C. Claims 2-5 and 8-9 are rejected as anticipated by Pascual et al. (Eur. J. Immunol. 23:1389-1392 (1993). This rejection was rendered moot by the cancellation of claims 1-19. Applicants respectfully submit that this rejection does not apply to new claims 22-37 (or claims 38-41).

The reference teaches Mab directed to rodent adipsin and not Factor D. The authors state at page 1390, section 3.1, last sentence of the first paragraph, "[t]he anti-r-adipsin IgG did not react with ^{125}I-human factor D". Indeed, this is why the human serum was depleted of **human Factor D** and restored with purified **mouse-r-adipsin.** Therefore, a claim to an antibody that specifically binds Factor D cannot be anticipated by antibodies that specifically bind mouse-r-adipsin and not human Factor D.

In view of this discussion, Applicants submit that Pascual et al. do not anticipate claims 22-37.

V. Rejection Under 35 U.S.C. § 103(a)

A. Claims 9, 14, and 17 have been rejected as unpatentable over Pascual et al. (either reference) in view of standard techniques in the art (Janeway et al.). This rejection was rendered moot by the cancellation of claims 1-19. However, this rejection should not apply to new claims 22-41 in view of the discussion above. The primary reference does not provide sufficient disclosure render new claims 33-37 unpatentable.

B. Claims 8, 13, 15, and 16 have been rejected as unpatentable over Pascual et al. (either reference) in view of U.S. Patent No. 5,861,156. This rejection

was rendered moot by the cancellation of claims 1-19. However, this rejection should not apply to new claims 22-41 in view of the discussion above. The primary reference does not provide sufficient disclosure render these claims unpatentable.

CONCLUSION

In view of the amendments and remarks presented above, Applicants submit that new claims 22-37 are allowable and request entry and rejoinder of claims 38-41. Claims 38-41 are of the same scope as claim 22 and therefore, also allowable.

Respectfully Submitted,

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were coated by adding 50 µl of purified human factor at 50 ng/ml overnight at room temperature. The low concentration of factor D for coating enabled the selection of high-affinity antibodies. After the coating solution was removed by flicking of the plate, 200 µl of BLOTTO (non-fat dry milk) in PBS was added to each well for one hour to block the non-specific sites. An hour later, the wells were then washed with a buffer PBST (PBS containing 0.05% Tween 20). Fifty microliters of culture supernatants from each fusion well were collected and mixed with 50 µl of BLOTTO and then added to the individual wells of the microtest plates. After one hour of incubation, the wells were washed with PBST. The bound murine antibodies were then detected by reaction with horseradish peroxidase (HRP) conjugated goat anti-mouse IgG (Fc specific) (Jackson ImmunoResearch Laboratories, West Grove, PA) and diluted at 1:2,000 in BLOTTO. Peroxidase substrate solution containing 0.1% 3,3,5,5 tetramethyl benzidine (Sigma, St. Louis, MO) and 0.0003% hydrogen peroxide (Sigma) was added to the wells for color development for 30 minutes. The reaction was terminated by addition of 50 µl of 2M H_2SO_4 per well. The OD at 450 nm of the reaction mixture was read with a BioTek ELISA Reader (BioTek Instruments, Winooski, VM).

The culture supernatants from the positive wells were then tested by two assays: i) inhibition of alternative pathway hemolysis of unsensitized rabbit RBCs by pre-titered human serum by the method described below; and ii) inhibition of formation of C3a by zymosan treated with human serum, as described below. The